UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/362,731	07/29/99	SAINT-REMY J	01699/P.UCB.

HM22/0717

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EXAMINER	
STROUP,C	

ART UNIT	PAPER NUMBER
1633	6

DATE MAILED: 07/17/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/362,731	Saint-Remy et al
Examiner	**Group Art Unit**
Stroup, Carrie	1633

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 3-7, 9-12, and 15-17* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3-7, 9-12, and 15-17* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Applicant's election of Group I in Paper No. 5, filed 5/3/00, is acknowledged. Election was made **without** traverse. Claims 2 and 8 have been cancelled. Claim 17 has been added. Claims 1, 3-7, 9-12, and 15-17 are currently pending in the present application.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Europe on 7/30/98. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

It is noted that only one copy of Figure 1 is included in the specification.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3-7, 9-12, and 15-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition and method of use in treating allergies in mice comprising an *Der pI or II* allergen antigenic determinant recognised by a B cell of a non-atopic individual bound via peptide linkage to an antigenic determinant of the antigen which triggers T cells activation in a T cell epitope, does not reasonably provide enablement for a compound, such as a medicament, pharmaceutical, cosmetical, beverage, food, or feed, and method of use in treating and preventing allergy in a human comprising at least one allergen antigenic determinant or an

secreted by a B cell of a non-atopic individual, and at least one antigenic determinant of an antigen different from said allergen which triggers a T cell activation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification provides an exemplification in which a 31 amino acid sequence (SEQ ID NO: 1 -15 a.a. of a T cell epitope of tetanus toxoid and 14 a.a. of a B cell epitope of Der p II- the *Dermatophagoides pteronyssinus* dust mite, connected by 2 glycines) when tested in vitro the B cell epitope was not recognized by IgE of IgG antibodies made by individuals sensitive to the native protein (atopic) but was recognized by IgG antiobodies of non-atopic individuals (Example 1) (pg 22-25). The specification also provides prophetic teachings on the administration of SEQ ID NO:1 and 14 to humans (pg 25-27), a variety of DNA vaccines encoding the disclosed peptides, a humanized animal model in SCID mice (pg 32), the formulation for "a cosmetic composition for skin hygiene" comprising any of the compounds of examples 1-3(pg 32), and the formulation for whey milk comprising any of the peptides of claims 1-3. The specification also provides a brief description of a Figure 1 wherein it discloses that Balb/c mice were immunized by two subcutaneous injections of rDer pII administered two weeks apart resulting in the production of antibodies to the peptide comprising Der pII amino acid 11-25. Further immunization with peptide 21-35 induced an immune response to such and a decrease of the binding of the peptide 11-25 epitope (Figure 1; pg 13, lines 16-33; pg 20, lines 8-26).

The specification fails to provide an enabling disclosure for the use of the claimed composition and method of treatment or prevention of allergies in any subject other than a mouse. Although the specification provides a prophetic teaching on the method of immunizing humans using the peptide encoded by SEQ ID NO: 1 in combination with a muramyl-dipeptide adjuvant via a subcutaneous route, said teachings do not equate to an enabling disclosure for a method of preventing or treating allergies in a human. The art of vaccination is highly unpredictable wherein the results obtained from an animal model and in vitro assays, such as the exemplified Balb/c mouse injected with SEQ ID

NO: 1 and 14 and Examples 1-4 for the binding of IgG and IgE antibodies to the B cell epitopes, do not necessarily equate to the level or type of immune response elicitied in humans following *in vivo* administration. Therefore, in the absence of specific teachings on the method of immunizing humans as extrapolated from, for example the prophetic teachings on a "humanized animal model" comprising a SCID mouse reconstituted with immunocompetent cells of human origin (Example 8, page 32), then one of skill in the art would be required to practice undue experimentation to use the claimed compositions and methods of use in a human such that any effective treatment of allergies would occur.

The specification also fails to provide an enabling disclosure for the use of a compound comprising any and all allergen antigenic determinants, such as the major antigen of Aspergillus fumigatus. The specification is limited in its entirety, to include the exemplification in Balb/c mice, to the use of Der pII antigenic determinants. The specification does not disclose the antigenic determinants of atopic and non-atopic individuals, nor the amounts which would be required to be administered per route of administration in mouse models such that a reduction in IgE antibodies would occur. Therefore, it would require undue experimentation by one of skill in the art to determine any allergen antigenic determinant recognized by a B cell of a non-atopic individual other than that of the *Dermatophagoides pteronyssinus* such that a reduction in allergic responses would occur upon immunization with said allergen.

The specification fails to provide an enabling disclosure for a compound and it use in the prevention of allergies. The specification fails to disclose, for example in the exemplification of the Balb/c mice immunized with Der pII of SEQ ID NO: 1, the level of allergic response to include the quantity of IgE antibodies and Th2 CD4+ helper T cells elicited upon challenge of a subject (e.g. Balb/c mouse) with Der pII, or with a Der pII antigen recognized by atopic individuals. Instead, the specification discloses the occurrence of a reduction in IgE antibodies which recognize the antigenic determinant with which the mouse was administered (p11). The specification does not demonstrate, though, that as per the theory of "clonal dominance" that the activation of B cells recognising other epitopes on the

same molecule is prevented by directing the allergic immune response in an atopic subject to alterative determinants (pg 19, lines 5-33). Therefore, in the absence of demonstrating the ability of the test mice to withstand challenge from exposure to Der pII, one of skill in the art would be required to practice undue experimentation such that use of the claimed invention would "prevent" an allergic response in a subject, mouse or human.

Lastly, the specification fails to provide an enabling disclosure for a cosmetical, beverage, food, or feed composition. Although the specification provides a formulation for the claimed compositions, it does not disclose its method of use, nor is such readily apparent to one of skill in the art. For example, it is unclear as to the rationale and method of use of a cosmetic composition for skin hygiene comprising the claimed anti-allergy compound. The specification has also not demonstrated the efficacy of the claimed compounds to treat allergies following topical or oral administration, wherein a high enough level of absorption into the circulatory system has not been demonstrated via these routes, nor would such be expected considering the ability of degradative enzymes to damage the peptides encoding the antigenic determinants. Therefore, one of skill in the art would be required to practice undue experimentation to utilize the disclosed compound via any formulation or route other than the exemplified subcutaneous or via direct intravenous injection.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

4. Claims 1, 3-7, 9-12, and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-7, 9-12, and 15-17 are unclear as to the metes and bounds of a compound consisting of "at least one allergen antigenic determinant which is recognised by a B cell or an antibody secreted by a B cell of a non-atopic

lines 3-5 of Claim 1. Does the compound consist of at least one allergen antigenic determinant of a non-atopic individual characterized by the fact that it is recognized by a B cell, or an antibody secreted by a B cell, of said non-atopic? Or does the compound consist of at least one allergen antigenic determinant which is recognized by a B cell of an atopic or non-atopic individual, or consisting of an antibody secreted by a B cell of a non-atopic individual?

No claims are allowed, although they are free of the prior art of record.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carrie Stroup whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached at (703) 308-0447. The fax phone number for this Group is (703) 308-8724.

Carrie Stroup

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